

### CDC Stage of HIV Disease

- Stage I: Acute HIV infection
- Stage II: Asymptomatic HIV
- Stage III: Early Symptomatic HIV
- Stage IV: Late Symptomatic HIV
- = A Constitutional Disease
- = B Neurological Disease
- = C Secondary Infections
- C1 AIDS defining
- C2 Other infections
- = D Secondary Cancers
- = E Other Conditions

### Clinical Staging of Oral Manifestations of HIV

Stage:	Adults and Adolescents (>15yo)	Children (<15yo):
1	No disease	No disease
2	Angular Chellitis, Recurrent oral ulcerations	Angular Chellitis, Linear gingival erythema, extensive warts, Recurrent oral ulcerations, Parotid enlarge
3	Persistent oral candidiasis, Oral hairy leukoplakia, Acute necrotizing ulcerative stomatitis, gingivitis, periodontitis	Persistent oral candidiasis (after 8wks), Oral hairy leukoplakia, Acute necrotizing ulcerative gingivitis or periodontitis.
4	Chronic (>1mo) orolabial HSV, Kaposi's sarcoma,	Chronic (>1mo) orolabial HSV, Karp'o's Sarcoma, Non-Hodgkin's lymphoma

### HIV-related Oral Lesions:

**Infectious:** - Fungal, Viral, Bacteria

**Neoplasms:** - Kaposi's Sarcoma, Non-Hodgkin's Lymphoma

**Other:** - Aphthous-like Ulcers, Lichenoid or drug reactions, Salivary Gland Disease

### Oral Candidiasis:

Erythematous Chelitis

Pseudomembranous

Angular

### Oral Ulcers:

-Herpes Simplex Infection -HPV Lesions

-Cytomegalovirus Infection -Lymphoma

-Aphthous Ulcers -Necrotizing ulcerative gingivitis/periodontitis

-Histoplasmosis -Necrotizing Stomatitis (NS)

There are many different causes of oral ulceration in patients with HIV infection = Herpes simplex infection, Varicella zoster infection. Accurate diagnosis and appropriate management of oral ulceration in patients with HIV infection generally result in complete healing of the ulceration.

### Aphthous Lesions Clinical Types

Topical Therapy:	Intralesional:	Systemic Therapy:
Topical Corticosteroids	Triamcinolone: 40 mg/ml (0.5 ml-1.0 ml injected bid)	Prednisone: 0.5-1.0 mg/kg qd x 7-10d, then taper
		Thalidomide: 200 mg PO qd

### Antiretroviral Cancer:

**NRTIs:** Nucleoside OR Nucleotide Reverse Transcriptase Inhibitors (Nukes)

**NNRTIs:** Non-nucleoside Reverse Transcriptase Inhibitors (non-nukes)

**PIs:** Protease Inhibitors

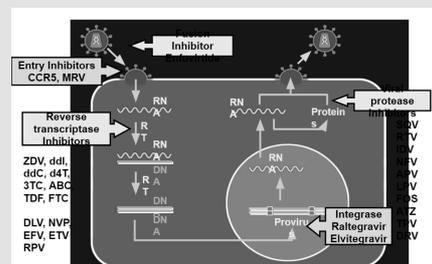
**Fusion Inhibitors**

**Chemokine Receptor Antagonists**

**Integrase Inhibitors**

See Life cycle of HIV

### Current Antiretroviral Targets



### Reverse Transcriptase Inhibitors:

#### Nucleoside Analogues

Zidovudine (AZT, ZDV) Didanosine (ddI) Zalcitabine (ddC) Stavudine (d4T) Lamivudine (3TC) Abacavir (ABC) Emtricitabine (FTC)

#### Non-nucleoside analogues:

Nevirapine (NVP) delavirdine (DLV) Efavirenz (EFV) etravirine (ETV) rilpivirine (RPV)

#### Nucleotide analogue

Tenofovir (TFV)

### Protease Inhibitors:

saquinavir (SQV)  
ritonavir (RTV)  
indinavir (IDV)  
nelfinavir (NFV)  
amprenavir (APV)  
lopinavir (LPV)  
fosamprenavir (FPV)  
atazanavir (ATV)  
tipranavir (TPV)  
darunavir (DRV)  
**dolutegravir (DTG)**

### Reverse Transcriptase Inhibitors:

#### Integrase Inhibitors

raltegravir (RAL)

elvitegravir (ELV)

#### Fusion Inhibitor:

fuzeon (T20)

#### Entry Inhibitors:

maraviroc (MVC)

### NRTIs Mechanism of Action:

#### Nucleoside Analogs (like AZT):

Analog of thymidine, cytosine or guanine

Triphosphorylated inside lymphocytes to active compound.

Incorporate into growing HIV viral DNA strand by reverse transcriptase.

#### Nucleotide

tenofovir (TDF)

#### Analogs:

does NOT need to be tri-phosphorylated only di-phosphorylated to activate compound.

After incorporation of NRTIs, viral DNA synthesis will be terminated.

### Non-nucleoside Reverse Transcriptase Inhibitors:

Agents directly bind to reverse transcriptase to inhibit transcription.

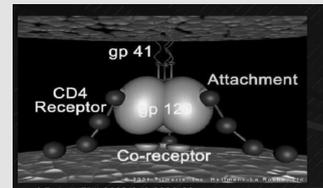
NNRTIs do not require phosphorylation to be active.

### Protease Inhibitors (PIs) MOA:

Protease enzyme cleaves HIV precursor proteins into active proteins that are needed to assemble a new, mature HIV virus.

PIs bind to protease preventing the cleavage and inhibiting the assembly of new HIV viruses.

### Fusion Inhibitor:



### Chemokine Receptor Antagonists:

Maraviroc (Selzentry)

CCR5 or CXCR4 receptors on cell surface

Virus will bind to one of the 2 receptors (some pt virus will bind to either receptors)

Maraviroc blocks viral entry at CCR5

Dosed 300mg BID= 150mg BID with P450 inhibitors. = 600mg BID with P450 inducers

### Integrase Inhibitors

Raltegravir (Isentress)

Dosed = 400mg BID (1tab BID)

No induction or inhibition on CYP450 enzymes or Pgp

Metabolized by UGT1A1 (glucuronidation) = Only affected by drugs that inhibit or induce UGTs (ie. rifampin)

